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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,940	12/05/2001	Jiangchun Xu	210121.427D3	8468

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EXAMINER	
ZHOU, SHUBO	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 09/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,940	XU ET AL.	
	Examiner	Art Unit	
	Shubo (Joe) Zhou	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,8-10,19 and 62-64* is/are pending in the application.

4a) Of the above claim(s) *64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,8-10,19,62 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/13/03, 6/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

DETAILED ACTION

Election/Amendments

1. Applicants' election of Group II (original claims 4-10, 18-22, 60-63, and 65-69) drawn to polynucleotides, and SEQ ID NO:313, in the response, filed 7/23/04, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 64, drawn to a recombinant protein, is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response filed 7/23/04.

Applicants' amendments to the claims are also acknowledged and entered. Claims 4, 8-10, 19, and 62-64 are currently pending, and claims 4, 8-10, 19, and 62-63 are under consideration.

Sequence Rules Compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because the sequences encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2) disclosed in Figures 8 and 11 are not followed by a sequence identifier (SEQ ID NO:X). Applicants are reminded that it is required that SEQ ID Nos be amended into the specification at each sequence, and that when a sequence is presented in a

drawing regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier must be used, either in the drawing or in the Brief Description of the Drawings. If any sequence encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2) is not listed in the current Sequence Listing, a new paper copy, a new CRF of a new Sequence Listing including these sequences, as well as a new statement under 37 CFR 1.821(f), are required. Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

Priority

3. It is noted that applicants claim domestic priority from a series of prior applications listed in the ADS filed 5/12/01. It is brought to applicants' attention that for the purpose of examination, priority has not been granted to all the applications filed before 1/15/1999, i.e. application 09/232,880 because the Office has not been able to determine by sequence searching that the elected invention including the sequence of SEQ ID NO: 313 was disclosed in those applications. Thus, for the purpose of examination, the earliest filing date of the applications for which priority has been granted is 09/232,880, filed 1/15/1999. Prior art published after those applications but before 1/15/1999 may have been cited in this Office action. Applicants are requested to provide evidence that the elected invention was disclosed in those prior applications if they wish to contest the citation of the intervening prior art.

Information Disclosure Statement

4. The Information Disclosure Statement filed 1/13/03 has been entered and the references therein have been considered except references AB, AE, BB, and CB, which are lined-through on the form PTO-1449 because these references are not in English. The IDS filed on 6/30/04 has also been entered and the references therein have been considered. A copy of each of the initialed forms of PTO-1449 is attached herein.

The citations/listings of publications and/or patents in various sections of the specification such as those on page 28 (of the electronic image of the specification filed 12/5/01 in the PAIR system), etc. are not a proper Information Disclosure Statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

5. The substitute specification filed 10/9/02 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) for a marked up version of the substitute specification has not been filed.

6. The specification filed 12/5/01 is objected to because of the following:

6a). The specification is not page-numbered.

6b). The statement of priority claim in the first paragraph of the specification needs to be updated to reflect the fact that the instant application is a divisional of the prior application 09/439,313, and the current status of the other prior US applications.

6c). It is noted that trademarks are used in this application, such as GENBANK™ (registered by United States Department of Health and Human Services). See the 31st page of the electronic image of the specification filed 12/5/01 in the PAIR system. Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

6d). The section of Brief Description of the Drawings (see pages from the 6th through the 25th of the electronic image of the specification filed 12/5/01 in the PAIR system) does not include Figure 11, and it is not noted that the figure is described in any other sections of the specification.

7. Appropriate correction is required.

Claim Rejections-35 USC § 101 and § 112

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph,

Written Description Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

See also the MPEP at §§ 2107 - 2107.02.

10. Claims 4, 8-10, 19, and 62-63 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The claims are drawn to nucleic acid molecules comprising the sequence of SEQ ID NO:313 or complement thereof, or vector and compositions comprising the nucleic acid molecules and recombinant cell comprising such vector. The claimed nucleic acid is not

supported by a specific asserted utility because the disclosed uses of the nucleic acids in the specification is not specific. For example, the specification asserts that the polynucleotides can be used as probes or primers to detect gene expression, or to modulate gene expression, etc. (see pages from the 32nd page to the 35th page of the electronic image of the specification filed 12/5/01 in the PAIR system). These are not specific uses for the claimed nucleic acids comprising SEQ ID NO:313 because they are generic to any nucleic acids that are expressed in an organism. Applicants list a number of possible uses for hundreds of different polynucleotides disclosed in the specification, but fail to assert a specific utility for the claimed nucleic acids of SEQ ID NO:313. None of the utilities is specifically linked to the claimed nucleic acids comprising the sequence of SEQ ID NO:313 or complement thereof.

Further, the claimed nucleic acid is not supported by a substantial utility. For example, the specification states that the nucleic acid can be used in "vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers", etc. (see page 1 of the electronic image of the specification filed 12/5/01 in the PAIR system). This is not deemed a substantial utility for the claimed polynucleotides. The specification only describes that the polynucleotide of SEQ ID NO:313 is obtained from a library of prostate tumor pools subtracted against pool of normal tissues. Although the polynucleotide is found to be over-expressed in prostate tumors than nonprostate tumors or normal tissues, it is also expressed in normal prostate tissues. See the 75th page of the electronic image of the specification filed 12/5/01 in the PAIR system. Therefore, one of ordinary skill in the art would have to perform further research to determine any function, if any, for the polynucleotide of SEQ ID NO:313, and how its function or pattern of expression is

specifically linked to prostate cancer development, etc. in order to possibly use it in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers, as asserted by applicants.

The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 USPQ 689 (1966), wherein the court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility (emphasis added). The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility...[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form there is insufficient justification for permitting an appellant to engross what may prove to be a broad field...a patent is not a hunting license...[i]t is not a reward for the search, but compensation for its **successful conclusion**.

It is clear that applicants have not arrived at the "successful conclusion" of what the actual function of the corresponding gene comprising the claimed polynucleotide or the polynucleotide itself are and how they are involved in the development of prostate cancer, and how it can be used for vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers. Without such knowledge, it would only serve as a starting point of further experimentation to arrive at the "successful conclusion" as expressed by the court.

Furthermore, neither the specification as filed nor any art of record discloses or suggests any property or activity for the claimed nucleic acid such that another non-asserted utility would be well established for the claimed nucleic acid or composition thereof.

11. The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 4, 8-10, 19, and 62-63 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention lacks a patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

13. Claims 4, 8-10, 19, and 62-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acids/polynucleotides comprising "a sequence set forth in SEQ ID NO:313", or vectors or composition comprising the polynucleotides. Since there is only one sequence set forth in SEQ ID NO:313, which is a 718-bps polynucleotide sequence (see the Sequence Listing), the limitation "a sequence set forth in SEQ ID NO:313" is interpreted to

be the full-length sequence of the 718 bps long polynucleotide. The specification discloses that SEQ ID NO:313 is not full-length, and it is used as probe for the search for full-length cDNA. Different splice variants have been found from the search. See the 97th page, Example 16, of the electronic image of the specification filed 12/5/01 in the PAIR system. Given the broad scope of the claims due to the use of the open language "comprising", and due to the fact that SEQ ID NO:313 is not a full-length cDNA, the claims are drawn to a genus: any nucleic acid that minimally contains the sequence of SEQ ID NO:313, including any full length cDNA molecule comprising the full ORF and any 5' and 3' UTR, etc. There is substantial variability among the species of polynucleotides or nucleic acids encompassed within the scope of the claims because the claimed SEQ ID NO:313 is only a fragment of these full-length cDNAs. Because the claimed genus encompasses species yet to be discovered, e.g. full-length cDNA constructs, etc., the mere disclosure in the specification of a species: the sequence of SEQ ID NO:313, does not provide an adequate description of the claimed genus.

In Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111), the court makes it clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.)

With the exception of the sequence of SEQ ID NO:313, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides/nucleic acids, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a

potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (See page 1115).

14. Claims 19 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)), the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation; (b) the amount of guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the predictability of the prior art; (g) the breadth of the claims; and (h) the relative skill in the art. The factors are analyzed for the instant case as follows:

(a) In the instant case, the amount of experimentation required by the skilled artisan in order to practice of making and using the claimed composition for pharmaceutical usage would require an unpredictable amount of experimentation for the following reasons:

(b)-(c) The claims are drawn to a pharmaceutical composition or a diagnostic kit comprising a polynucleotide comprising the sequence of SEQ ID NO:313. The instant specification does not provide an explicit definition for the term "pharmaceutical". According to Steadman's Medical Dictionary (22nd Edition, 1972), "pharmaceutical" means "relating to pharmacy or to pharmaceutics" (page 952). In the same dictionary, "pharmacy" is defined as: "the practice of preparing and dispensing drugs", and "drug" is defined as "A therapeutic agent; any substance, other than food, used in the prevention, diagnosis, alleviation, treatment, or cure of disease in man and animal (page 378)." Thus, "a pharmaceutical use" would be any use, other than as food, wherein a substance is used on or in the body to prevent, diagnose, alleviate, treat, or cure a disease in humans or animals. In the specification, applicants state that the claimed polynucleotides can be used in "vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers" (page 1 of the electronic image of the specification filed 12/5/01 in the PAIR system). Therefore, in the instant application, a pharmaceutical use is for "vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers". As set forth in the previous section, the specification only describes that the polynucleotides of SEQ ID NO:313 is obtained from a library of prostate tumor pools subtracted against pool of normal tissues. Although the polynucleotide of SEQ ID NO:313 is found to be over-expressed in prostate including prostate tumors compared to other tissues, the expression is lower and in fewer prostate tumors compared to several other polynucleotides. See the 75th page of the electronic image of the specification filed 12/5/01 in the PAIR system. Thus, the specification describes that the polynucleotide of SEQ ID NO:313 is present in both normal prostate and prostate tumors, and it is not overexpressed in the latter compared to the former. Clearly, the polynucleotide of SEQ ID NO:313 is at best a prostate specific, but not prostate tumor specific polynucleotide. The specification does not provide guidance as to how to use such

a polynucleotide, which is not differentially expressed in prostate tumor compared to normal prostate tissue, in "vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers", nor does it provide any working example for such usage.

(d)-(h) The nature of the invention, i.e. a pharmaceutical composition or a diagnostic kit comprising a polynucleotide comprising the sequence of SEQ ID NO:313 for use in "vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers", is complex. The prior art does not teach or fairly suggest such a pharmaceutical composition or such diagnostic kit for such usages. However, the idea of using cancer vaccines for treating or preventing cancer has been around for years, albeit no successful test has been done. Ezzell (The J. NIH Research, Vol. 7, pages 46-49, 1995) reviews recent progress in the field of cancer immunotherapy. He reviewed that several tumor specific antigens including MAGE-1, which is a tumor specific peptide that is expressed by cells of pigmented skin cancer melanoma but not by normal melanocytes, the skill cell that produce the pigment, have been discovered and researchers are attempting to use such peptides in cancer vaccines. See pages 46-47. He states that the optimal cancer vaccine will consist of several tumor-specific antigens so that cancer cells cannot escape the anti-tumor response by developing a single mutation" (page 48). Ezzell cites a cancer immunotherapy scientist from the National Cancer Institute, Steve Rosenberg, "there are a lot of possibilities why some people respond and other do not", and "there is also enormous variability among patients and their expression of antigens on tumors". Ezzell concludes that 'no one is very optimistic that a single peptide or a virus carrying the gene encoding that peptide will trigger an immune response strong enough to

eradicate tumors or even to prevent the later growth of micrometastases among patients". See page 48. It is clear that the field of cancer immunotherapy is only at its beginning, and is highly unpredictable. In order to possible use a peptide or a polynucleotide encoding a peptide, the minimum requirement is that it is tumor specific, i.e. in the case of prostate cancer, only expressed in prostate cancer, not in normal prostate tissue. In the instant application, the polynucleotide of SEQ ID NO:313 is only disclosed as a prostate specific, not prostate tumor specific. As to diagnosis of prostate cancer, the art is also unpredictable. Aspinall (Journal of Urology, Vol. 154, pages 622-628, August 1996) reports that while the increased level of serum PSA (prostate specific antigen) has been well known to be associated with prostate cancer, they demonstrate that the not only the level of PSA is not elevated in prostate cancer tissues, is the level actually lower in prostate cancer tissue than in nonmalignant prostate. See page 622, Abstract. Obviously, simply demonstrating something that is present in prostate tumor as well as in normal prostate, as is the case in the instant application, is not sufficient to demonstrate it can be used as a diagnostic marker.

The skilled practitioner would first turn to the instant specification for guidance in practice of using the polynucleotide of SEQ ID NO:313 for vaccine for treating or preventing prostate cancer, or for a diagnostic marker. However, the specification does not provide sufficient guidance of practicing the invention. As such, the skilled practitioner would turn to the prior art for such guidance. However, the prior art does not teach the polynucleotide and such uses thereof. Finally, said practitioner would have to turn to trial and error experimentation for practicing using the polynucleotide for a vaccine or for a diagnostic marker for prostate

cancer without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

Claim Rejections-35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> *A person shall be entitled to a patent unless –*
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claim 8 is rejected under 35 U.S.C. § 102(b) as being anticipated by NCI-CGAP (Database sequence, GenBank accession No. AA578773, 9/12/1997).

Claim 8 is drawn to an isolated polynucleotide complementary to a polynucleotide comprising the sequence of SEQ ID NO:313.

Absent an explicit definition for the term "complementary" in the specification, it is broadly interpreted as being both completely and partly complementary. It is known in the art that a polynucleotide can be completely or partially complementary to another polynucleotide. For example, Au-Young et al. (WO 00/18922) state that "the term 'complementary' or 'complementarity' refers to the natural binding of polynucleotides by base paring", and "complementarity between two single-stranded molecules may be 'partial', such that only some of the nucleic acids binds, or it may be 'complete', such that total complementarity exists between the single stranded molecules." See page 13, lines 11-19.

NCI-CGAP at Database GenBank accession No. AA578773 discloses a polynucleotide sequence that has long stretches of sequences that matches the sequence of the instant SEQ ID NO:313. See the attached sequence alignment between the two sequences. Since the sequence by NCI-CGAP is obtained from an isolated double stranded cDNA clone in vector pAMP10 in host cell DH10B (see what is disclosed in "FEATURES" of the database accession), it would have been readily recognized by one skilled in the art that the sequence of the other strand that is completely complementary to the sequence of AA578773 is partially complementary to the sequence of SEQ ID NO:313.

17. Claim 8 is rejected under 35 U.S.C. § 102(a) as being anticipated by Bussemakers MJG (WO 98/45420-A1, 10/15/1998).

Claim 8 is drawn to an isolated polynucleotide complementary to a polynucleotide comprising the sequence of SEQ ID NO:313.

Absent an explicit definition for the term "complementary" in the specification, it is broadly interpreted as being both completely and partly complementary. It is known in the art that a polynucleotide can be completely or partially complementary to another polynucleotide. For example, Au-Young et al. (WO 00/18922) state that "the term 'complementary' or 'complementarity' refers to the natural binding of polynucleotides by base paring", and "complementarity between two single-stranded molecules may be 'partial', such that only some of the nucleic acids binds, or it may be 'complete', such that total complementarity exists between the single stranded molecules." See page 13, lines 11-19.

Bussemakers discloses an isolated cDNA sequence of 820 bps (PCA3, which is the same sequence as disclosed in database Geneseq acc. NO. AAV62429) that has long stretches of sequences that matches the sequence of the instant SEQ ID NO:313. See the attached sequence alignment between the two sequences. Since the sequence by Bussemakers is obtained from an

isolated double stranded cDNA PCA3 (see page 1, abstract), it would have been readily recognized by one skilled in the art that the sequence of the other strand that is completely complementary to the sequence of AA578773 is partially complementary to the sequence of SEQ ID NO:313. Further, Bussemakers discloses also the sequence complementary strand of PCA3. See page 26, lines 27-28.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

20. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of

the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shubo (Joe) Zhou, Ph.D. 

Patent Examiner

Continuation of Attachment(s) 6). Other:

a) Sequence Alignment between AA578773 and SEQ ID NO:313

b) Sequence Alignment between AAV62429 and SEQ ID NO:313 .

AA578773 and SEQ ID NO: 313

	78	37	5.2	612	29	CE819682
	79	37	5.2	1101	29	CNS00FOO
	80	37	5.2	1101	29	CNS010CR
c	81	37	5.2	1201	13	BX375913
	82	36.8	5.1	573	28	AZ639671
c	83	36.8	5.1	747	14	CK142144
	84	36.8	5.1	795	13	BU278635
	85	36.8	5.1	864	28	AZ538148
	86	36.8	5.1	990	13	BX382345
	87	36.8	5.1	1201	13	BX406374
c	88	36.8	5.1	1401	29	CG754213
c	89	36.6	5.1	304	29	CE225378
	90	36.6	5.1	402	14	CB768924
	91	36.6	5.1	483	13	BX391153
c	92	36.6	5.1	577	29	CE642724
	93	36.6	5.1	669	29	CE306789
	94	36.6	5.1	671	29	CG913525
	95	36.6	5.1	999	13	BX380865
	96	36.6	5.1	1201	9	AL546457
c	97	36.6	5.1	1201	13	BX403620
c	98	36.4	5.1	475	13	BY561537
c	99	36.4	5.1	482	28	AQ701841
	100	36.4	5.1	550	14	CA856833

CE819682	tigr-gss-
AL070854	Drosophil
AL098805	Drosophil
BX375913	BX375913
AZ639671	1M0501I17
CK142144	AGENCOURT
BU278635	603577165
AZ538148	ENTDU24TR
BX382345	BX382345
BX406374	BX406374
CG754213	P049-3-C1
CE225378	tigr-gss-
CB768924	AMGNNUC:S
BX391153	BX391153
CE642724	tigr-gss-
CE306789	tigr-gss-
CG913525	ZMMBBb037
BX380865	BX380865
AL546457	AL546457
BX403620	BX403620
BY561537	BY561537
AQ701841	HS_5401_A
CA856833	PfESTOac4

ALIGNMENTS

RESULT 1
AA578773
LOCUS AA578773 402 bp mRNA linear EST 12-SEP-1997
DEFINITION nh24a04.s1 NCI_CGAP_Pr1 Homo sapiens cDNA clone IMAGE:953262, mRNA sequence.
ACCESSION AA578773
VERSION AA578773.1 GI:2356957
KEYWORDS EST.
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 402)
AUTHORS NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap.
TITLE National Cancer Institute, Cancer Genome Anatomy Project (CGAP), Tumor Gene Index
JOURNAL Unpublished (1997)
COMMENT Contact: Robert Strausberg, Ph.D.
Email: cgapbs-r@mail.nih.gov
Tissue Procurement: W. Marston Linehan, M.D., Rodrigo Chuaqui, M.D., Michael Emmert-Buck, M.D., Ph.D.
cDNA Library Preparation: David B. Krizman, Ph.D.
cDNA Library Arrayed by: Genome Systems Inc., Greg Lennon, Ph.D.
DNA Sequencing by: Washington University Genome Sequencing Center
Clone distribution: NCI-CGAP clone distribution information can be found through the I.M.A.G.E. Consortium/LLNL at: www-bio.llnl.gov/bbrp/image/image.html
Insert Length: 565 Std Error: 0.00
Seq primer: -40m13 fwd. ET from Amersham
High quality sequence stop: 373.
FEATURES Location/Qualifiers
source 1. .402
/organism="Homo sapiens"
/mol_type="mRNA"
/db_xref="taxon:9606"
/clone="IMAGE:953262"
/sex="Male"
/dev_stage="45 years old"
/lab_host="DH10B"
/clone_lib="NCI_CGAP_Pr1"
/note="Vector: pAMP10; Site_1: Not1; Site_2: EcoRI; 1st strand cDNA was primed with oligo(dT)17 on 50 ng of DNAse-treated, total cellular RNA obtained from 5,000-10,000 microdissected, histologically normal prostate epithelial cells. Double-stranded cDNA was ligated to EcoRI adaptors, 5 cycles of PCR applied to the cDNA with an adaptor-specific primer, and the resulting PCR product subcloned into pAMP10 by the UDG-cloning method (Life Technologies). Average insert size is 600 bp. NOTE: Not directionally cloned. This library was constructed by David Krizman."

ORIGIN

Query Match 22.8%; Score 163.8; DB 9; Length 402;
Best Local Similarity 94.7%; Pred. No. 2.9e-34;
Matches 213; Conservative 0; Mismatches 7; Indels 5; Gaps 4;

```
Qy      376 CAGGAAAACAGATCCTGTTGTGGATATTTATTTGAACGGGATTACAGATTTGAAATGAAG 435
            ||||||||||||||||||||||||||||| |||||||||||||||||||||||||||||||
Db        8 CAGGAAAACAGATCCTGTTGTGGATATATATTTGAACGGGATTACAGATTTGAAATGAAG 67

Qy      436 TCACAAAGTGAGCATTACCAATGAGAGGAAAACAGACGAGAAAATCTTGATGG-TTCACA 494
            |||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||
Db       68 TCACAAAGTGAGCATTACCAATGAGAGGAAAACAGACGAGAAAATCTTGATGGCTTCACA 127

Qy      495 AGACATGCAACAAACAAAATGGAATACTGTGATGACACGAG--CAGCCAACTGGGGAGGA 552
            |||||||||||||||||||||||||||||||||||||||| ||| | | ||||||||||
Db      128 AGACATGCAACAAACAAAATGGAATACTGTGATGACATGAGGCAGCCAAGCTGGGGAGGA 187

Qy      553 GAT-ACCACGGGGCAGA-GGTCAGGATTCTGGCCCTGCTGCCTAA 595
            ||| |||||||||||||| ||||||||||||||||||||||||||
Db      188 GATAACCACGGGGCAGAGGGTCAGGATTCTGGCCCTGCTGCCTAA 232
```

RESULT 2
BF373406
LOCUS BF373406 167 bp mRNA linear EST 24-NOV-2000
DEFINITION IL2-FT0159-070800-120-H01 FT0159 Homo sapiens cDNA, mRNA sequence.
ACCESSION BF373406
VERSION BF373406.1 GI:11335431
KEYWORDS EST.
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 167)
AUTHORS Dias Neto,E., Garcia Correa,R., Verjovski-Almeida,S., Briones,M.R., Nagai,M.A., da Silva,W. Jr., Zago,M.A., Bordin,S., Costa,F.F., Goldman,G.H., Carvalho,A.F., Matsukuma,A., Baia,G.S., Simpson,D.H., Brunstein,A., deOliveira,P.S., Bucher,P., Jongeneel,C.V., O'Hare,M.J., Soares,F., Brentani,R.R., Reis,L.F., de Souza,S.J. and Simpson,A.J.
TITLE Shotgun sequencing of the human transcriptome with ORF expressed sequence tags
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 97 (7), 3491-3496 (2000)
MEDLINE 20202663
PUBMED 10737800
COMMENT Contact: Simpson A.J.G.
Laboratory of Cancer Genetics
Ludwig Institute for Cancer Research
Rua Prof. Antonio Prudente 109, 4 andar, 01509-010, Sao Paulo-SP, Brazil
Tel: +55-11-2704922
Fax: +55-11-2707001
Email: asimpson@ludwig.org.br
This sequence was derived from the FAPESP/LICR Human Cancer Genome Project. This entry can be seen in the following URL (http://www.ludwig.org.br/scripts/gethtml2.pl?t1=IL2&t2=IL2-FT0159-070800-120-H01&t3=2000-08-07&t4=1)
Seq primer: puc 18 forward
High quality sequence stop: 167.
FEATURES Location/Qualifiers
source 1. .167
/organism="Homo sapiens"
/mol_type="mRNA"
/db_xref="taxon:9606"
/dev_stage="Adult"
/clone_lib="FT0159"

29-JUN-2001; 2001US-00895814.
10-DEC-2001; 2001US-00012896.
09-MAY-2002; 2002US-00144678.

(CORI-) CORIXA CORP.

Xu J, Stolk JA, Kalos MD;

WPI; 2003-756193/71.

New isolated polypeptide for use in a vaccine for stimulating an immune response, or for treating or diagnosis cancer, preferably prostate cancer.

Example 16; Page; 101pp; English.

The invention relates to an isolated polypeptide comprising no more than 11-542 amino acids of ADB13563 comprising a sequence ADB14487. The peptides comprise a fragment ADB13563 of that contain naturally processed T-cell epitopes for 3 class I major histocompatibility complex (MHC) alleles. ADB13563 is a polypeptide encoded by a human prostate specific cDNA, one of 648 disclosed as new. Also included are nucleic acids encoding the proteins and peptides, expression vectors, a host cell transformed with the vector, an isolated antibody (or antigen binding fragment) that specifically binds to the protein or peptide, detecting the presence of a cancer in a patient (comprising contacting a patient sample with a binding agent that binds to the peptides or a polypeptide appearing as ADB13558, detecting the amount of polypeptide that binds to the agent and comparing the amount of polypeptide to a predetermined cut-off value to determine the presence of cancer), a fusion protein comprising the peptides or proteins, stimulating or expanding T cells specific for a tumour protein comprising contacting T cells with the peptides or the isolated T cell population, treating prostate cancer in a patient comprising administering a composition comprising the peptides, nucleic acids, antibodies or compounds, determining the presence of a cancer in a patient and treating prostate cancer in a patient comprising incubating cluster of differentiation (CD4+) and/or CD8+ T cells isolated from a patient with the peptides or antigen presenting cells that express (the peptides so that the T cells proliferate, and administering the proliferated T cells to the patient. The peptides (or an oligonucleotide that hybridises to nucleic acid encoding them), is used to detect the presence of cancer in a patient. The peptides, nucleic acids encoding, or antigen-presenting cells expressing the nucleic acid, are used to stimulate or expand T cells specific for a tumour protein. The peptides, nucleic acids, antibodies, fusion proteins, T cell populations or antigen presenting cells are used to stimulate an immune response or treat prostate cancer in a patient. The present sequence is a known cDNA showing sequence similarity to one of the disclosed human prostate specific cDNAs. Note: Except where otherwise indicated, the sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from USPTO at seqdata.uspto.gov/sequence.html?DocID=20030185830.

Sequence 812 BP; 198 A; 189 C; 169 G; 256 T; 0 U; 0 Other;

Query Match 71.5%; Score 513.2; DB 9; Length 812;
Best Local Similarity 97.3%; Pred. No. 1.3e-147;
Matches 585; Conservative 0; Mismatches 9; Indels 7; Gaps 6;

```
Qy          1 GGAGATTTGTGTGGTTTGCAGCCGAGGGAGACCAGGAAGATCTGCATGGTGGGAAGGACC 60
              ||||||||||||  ||||||||||||||||||||||||||||||||||||||||||||||
Db        791 GGAGATTTGTGTGG-CTGCAGCCGAGGGAGACCAGGAAGATCTGCATGGTGGGAAGGACC 733

Qy         61 TGATGATACAGAGGTGAGAAATAAGAAAGGCTGCTGACTTTACCATCTGAGGCCACACAT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        732 TGATGATACAGAGGTGAGAAATAAGAAAGGCTGCTGACTTTACCATCTGAGGCCACACAT 673

Qy        121 CTGCTGAAATGGAGATAATTAACATCACTAGAAACAGCAAGATGACAATATAATGTCTAA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        672 CTGCTGAAATGGAGATAATTAACATCACTAGAAACAGCAAGATGACAATATAATGTCTAA 613

Qy        181 GTAGTGACATGTTTTTGCACATTTCCAGCCCTTTTAAATATCCACACACACAGGAAGCAC 240
              ||||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
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AAV62429 cDNA SEQ ID NO: 513

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Db        612 GTAGTGACATGTTTTTGCACATTTCCAGCCCCTTTAAATATCCACACACACAGGAAGCAC 553

Qy        241 AAAAGGAAGCACAGAGATCCCTGGGAGAAATGCCCGGCCGCCATCTTGGGTCATCGATGA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        552 AAAAGGAAGCACAGAGATCCCTGGGAGAAATGCCCGGCCGCCATCTTGGGTCATCGATGA 493

Qy        301 GCCTCGCCCTGTGCCTGNTCCCGCTTGTGAGGGAAGGACATTAGAAAATGAATTGATGTG 360
              |||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||
Db        492 GCCTCGCCCTGTGCCTGGTCCCGCTTGTGAGGGAAGGACATTAGAAAATGAATTGATGTG 433

Qy        361 TTCCTTAAAGGAT-GGCAGGAAAACAGATCCTGTTGTGGATATTTATTTGAACGGGATTA 419
              |||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||
Db        432 TTCCTTAAAGGATGGGCAGGAAAACAGATCCTGTTGTGGATATTTATTTGAACGGGATTA 373

Qy        420 CAGATTTGAAATGAAGTCACAAAGTGAGCATTACCAATGAGAGGAAAACAGACGAGAAAA 479
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        372 CAGATTTGAAATGAAGTCACAAAGTGAGCATTACCAATGAGAGGAAAACAGACGAGAAAA 313

Qy        480 TCTTGATGG-TTCACAAGACATGCAACAAACAAAATGGAATACTGTGATGACACGAG--C 536
              ||||||||| |||||||||||||||||||||||||||||||||||||||||||| |||
Db        312 TCTTGATGGCTTCACAAGACATGCAACAAACAAAATGGAATACTGTGATGACATGAGGCA 253

Qy        537 AGCCAACTGGGGAGGAGAT-ACCACGGGGCAGA-GGTCAGGATTCTGGCCCTGGTGCCTA 594
              | | ||||||||||||||| |||||||||||||| ||||||||||||||||||||||||
Db        252 GCCAAGCTGGGGAGGAGATAACCACGGGGCAGAGGGTCAGGATTCTGGCCCTGCTGCCTA 193

Qy        595 A 595
              |
Db        192 A 192
```

RESULT 21
AAV62429
ID AAV62429 standard; cDNA; 820 BP.
XX
AC AAV62429;
XX
DT 30-DEC-1998 (first entry)
XX
DE Prostate cancer antigen (PCA3) cDNA splice variant 3.
XX
KW Prostate cancer antigen cDNA splice variant 3; PCA3; prostatic cancer;
KW PC; ds.
XX
OS Homo sapiens.
XX
PN WO9845420-A1.
XX
PD 15-OCT-1998.
XX
PF 09-APR-1998; 98WO-CA000346.
XX
PR 10-APR-1997; 97US-0041836P.
XX
PA (DIAG-) DIAGNOCURE INC.
XX
PI Bussemakers MJG;
XX
DR WPI; 1998-568347/48.
XX
PT New nucleic acid encoding prostate cancer antigen 3 - for diagnosis,
PT prevention and treatment of prostatic cancer.
XX
PS Claim 4; Page 77-78; 111pp; English.
XX
CC The present sequence represents the prostate cancer antigen (PCA3) cDNA
CC splice variant 3 sequence comprising of exons 1, 3, and 4a of the PCA3
CC gene. The PCA3 cDNA splice variant 3 sequence, isolated from a human
CC primary prostatic tumour tissue cDNA library, was found in approximately
CC 15% of the cDNA clones isolated. The invention claims for PCA3 cDNA
CC variants and the proteins they encode. The invention also claims for
CC antibodies against PCA3 protein. The antibodies are claimed to be useful
CC for detecting PCA3 protein in immunoassay tests, for diagnosing,